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Epidemiology of Multiple Myeloma

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Multiple myeloma, a plasma cell tumor arising in the bone marrow, is a rare cancer with an elusive etiology. In the United States multiple myeloma is estimated to account for approximately 1 percent of all diagnosed cancers and 2 percent of all cancer deaths.[1] According to estimates provided by the American Cancer Society, approximately 5800 men and 5400 women were expected to die from multiple myeloma in the United States during 2000.[1] The lifetime risk of being diagnosed with myeloma in the United States is 0.85 percent for black men, 0.61 percent for white men, 0.99 percent for black women, and 0.50 percent for white women.[2]

DESCRIPTIVE EPIDEMIOLOGY

U.S. Mortality Patterns

Based on data from the National Center for Health Statistics, 1950–1997, age-adjusted mortality rates (using the 1970 U.S. standard) among whites almost tripled, reaching highs of 3.6 per 100,000 and 2.4 per 100,000 among men and women, respectively, in 1995 to 1997 (Figure 26–1). Rates among nonwhites (consisting of the combined group of blacks, Asians and Pacific Islanders, and American Indians and Alaskan Natives) more than quadrupled during this 47-year period, reaching a high of 4.4 per 100,000 among women in 1995 to 1997 and 6.2 per 100,000 among men in 1990 to 1994 before falling to 5.9 in 1995 to 1997. These increases are among the highest observed for any cancer during this time period.[2]

Rates specific for blacks, available since the early 1970s, are higher than rates for all nonwhites combined, and the rates increased more rapidly, with the highest rates for males (7.5 per 100,000) observed in 1990 to 1994 and for females (5.4 per 100,000) in 1995 to 1997.

To evaluate whether the increases in multiple myeloma mortality during the past five decades were confined to certain age groups or specific time periods, rates were examined according to age group and year of birth (Figure 26–2). For all race and sex categories, the increases in mortality occurred primarily among individuals aged 55 years and older, with the most marked changes occurring in the two oldest age groups, 75 to 84 and over 85. The risk of dying from multiple myeloma rose steadily among individuals born in the middle to late 1800s and early 1900s, whereas more recent birth cohorts experienced little change in risk. Whether the substantial rises among persons born prior to the early 1900s were due to improving diagnosis or to increasing risk due to environmental exposures is not well understood. It is noteworthy that rates among persons born more recently have not risen in a similar fashion.

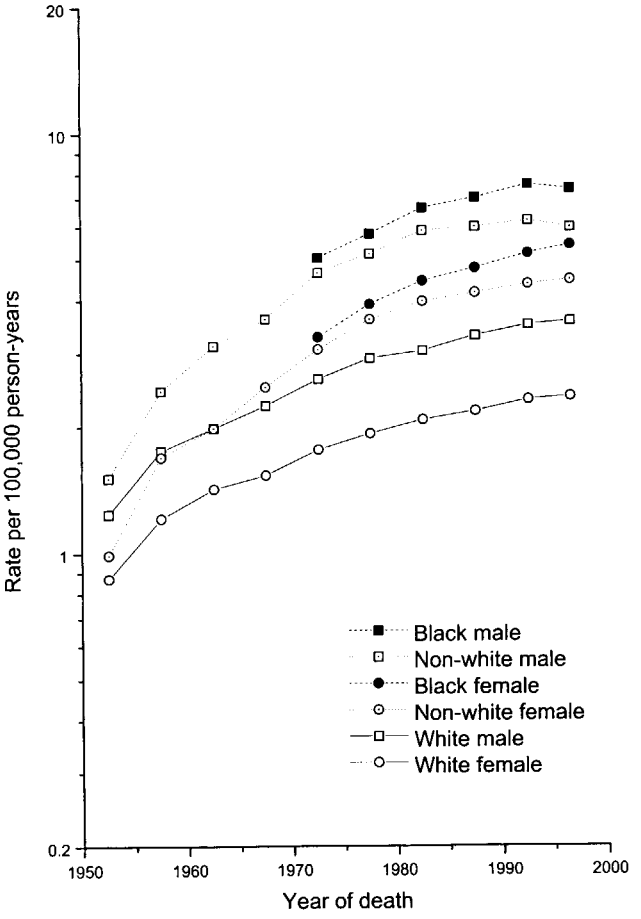

Figure 26–1. Age-adjusted (1970 U.S. standard) multiple myeloma mortality trends in the United States by race and sex, 1950–54 to 1990–94, 1995–97.

U.S. Survival Patterns

Survival data based on follow-up evaluation of newly diagnosed cases since the 1970s are available from the Surveillance, Epidemiology, and End Results (SEER) program.[2] Presented are data from nine SEER population-based cancer registries surveying approximately 10 percent of the U.S. population. Although survival among patients diagnosed with multiple myeloma is poor for all race and sex groups, significant improvements in the 5-year relative survival rates have occurred over the past two decades, from 24.5 percent among patients diagnosed during 1974 to 1976 to 28.5 percent among those diagnosed during 1989 to 1996 (data not shown).[2]

The 5-year relative survival rates by age at diagnosis, race, and sex for patients diagnosed during 1989 to 1996 are pre-

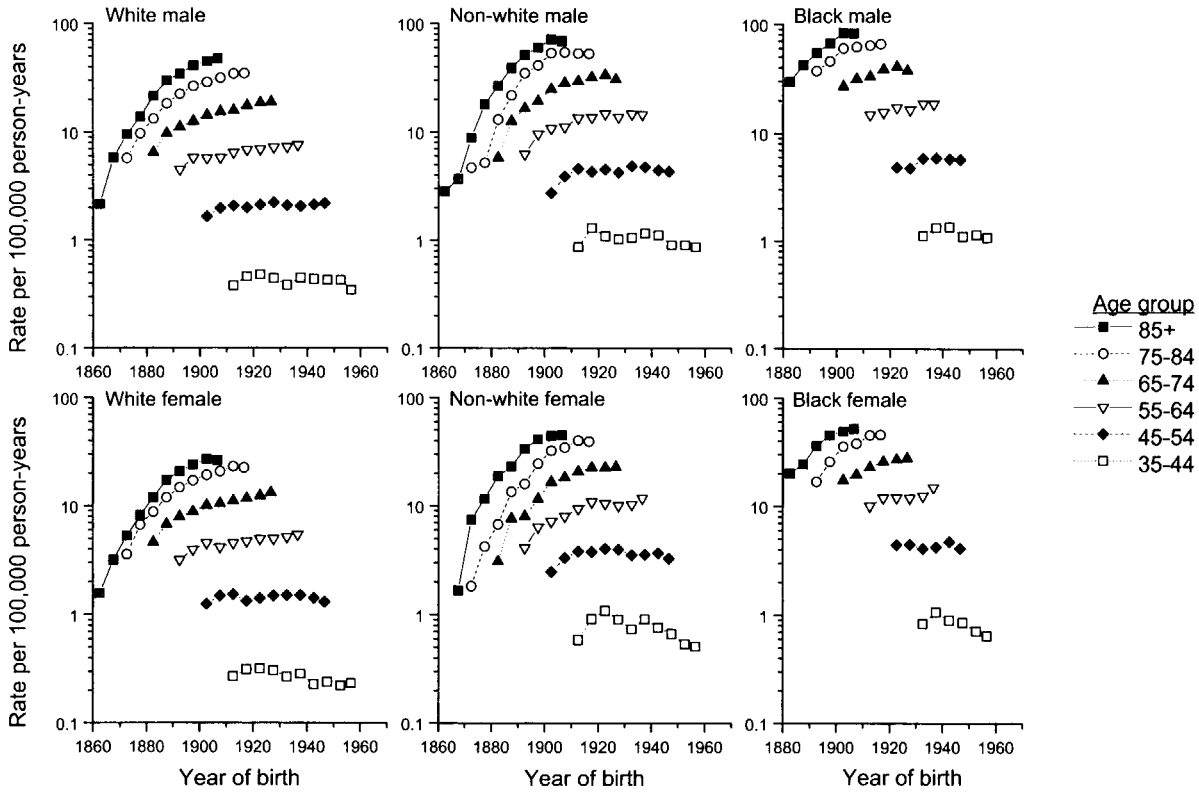

Figure 26–2. Age-specific multiple myeloma mortality trends in the United States by sex, race, age group, and cohort year of birth, 1860 to 1970.

sented in Table 26–1.[2] For all race and sex groups, survival was more favorable among those diagnosed at younger ages than among the elderly. The 5-year relative survival rates for all myeloma patients combined in the age groups under 45, 45 to 54, 55 to 64, 65 to 74, and 75 years or older were 47, 42, 33, 27, and 19 percent, respectively, with rates of 37 versus 23 percent among those under versus those older than age 65. Survival rates for all ages combined were higher for blacks than for whites (30.9 versus 27.8 percent) and for males than for females (29.7 versus 27.2 percent).

Table 26–1. Five-Year Relative Survival Rates (Percent) Among Patients Diagnosed with Multiple Myeloma in the U.S. Nine SEER Areas During 1989 to 1996 by Age at Diagnosis, Sex, and Race[a]

	Whites		Blacks	
Age at Diagnosis (yr)	**Males**	**Females**	**Males**	**Females**
<45	42.1	47.7	52.1	49.1
45–54	40.7	41.3	44.1	42.9
55–64	34.8	32.0	37.8	30.1
65–74	25.5	26.8	26.8	24.0
75+	18.8	17.8	21.1	17.6
All ages	28.8	26.7	34.2	28.0
Under 65	37.2	36.5	42.6	36.7
65 and older	22.9	22.3	25.0	21.2

Source: SEER Cancer Statistics Review 1973 to 1997, National Cancer Institute, 2000.

[a] SEER, National Cancer Institute. Based on data from nine population-based registries in Connecticut, New Mexico, Utah, Iowa, Hawaii, Atlanta, Detroit, Seattle–Puget Sound, and San Francisco–Oakland. Rates are based on follow-up study of patients through 1997.

U.S. Incidence Patterns

In contrast to the notable increases in age-adjusted mortality rates during 1950 to 1997, age-adjusted incidence rates (using the 1970 U.S. standard) rose only modestly in the nine SEER areas during 1973 to 1997 (Figure 26–3). Rates were highest among black men, followed by black women and then white men; they were lowest among white women. Age-adjusted incidence rates among white men peaked at 5.4 per 100,000 in 1988 to 1992 and then declined to 5.1 per 100,000 in 1993 to 1997, whereas rates among black men increased to 11.4 per 100,000 in 1993 to 1997. Rates changed little among white women, but they rose steadily among black women, reaching 8.6 per 100,000 in 1993 to 1997.

Age-specific incidence rates for multiple myeloma for 1973 to 1997 are presented in Figure 26–4. Among white men and black women, incidence rates rose steadily with age, whereas they increased and then decreased for white women and black men aged 85 and older. Rates consistently were higher among blacks than whites and among males than among females.

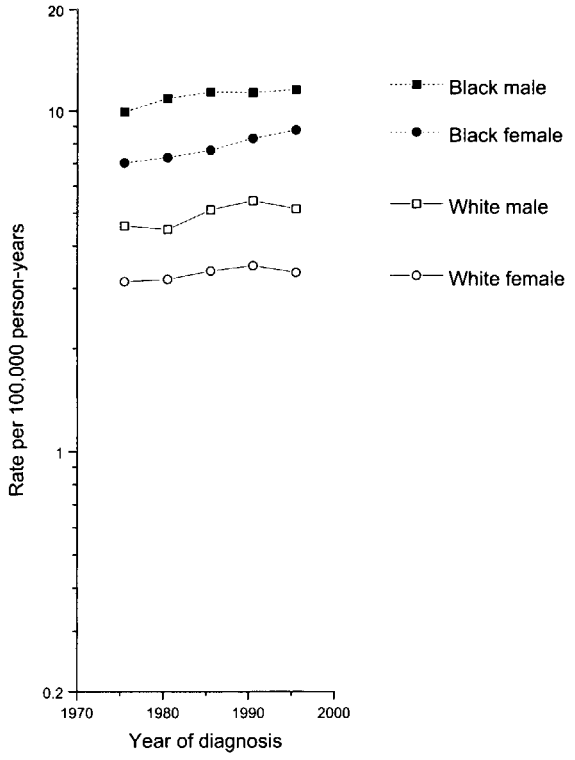

Figure 26–3. Age-adjusted (1970 U.S. standard) multiple myeloma incidence trends in the U.S. nine SEER areas by race and sex, 1973–77 to 1993–97.

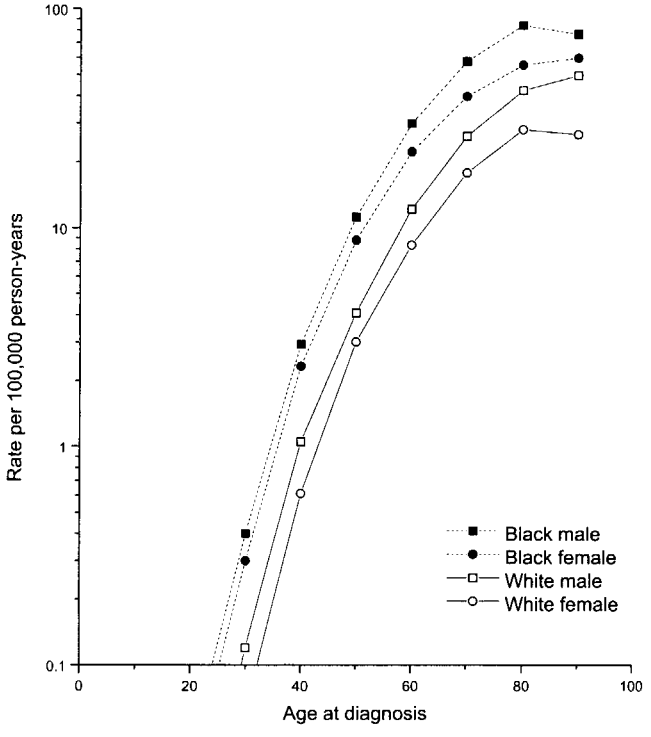

Figure 26–4. Age-specific multiple myeloma incidence rates in the U.S. nine SEER areas by race and sex, 1973 to 1997.

Table 26–2. Age-Adjusted (1970 U.S. Standard) Multiple Myeloma Incidence and Mortality Rates in the U.S. 11 SEER areas by race/ethnicity and sex, 1990–1997[a]

	Incidence Rate per 100,000 Persons[b]		Mortality Rate per 100,000 Persons[c]	
Race/Ethnicity	**Males**	**Females**	**Males**	**Females**
All races	5.6	3.7	3.8	2.6
White	5.2	3.4	3.5	2.3
White Hispanic	5.2	3.3	3.0	2.1
White Non-Hispanic	5.2	3.4	3.5	2.3
Black	11.2	8.3	7.4	5.2
Asian/Pacific Islander	3.5	2.2	1.8	1.2
American Indian	3.5	2.4	—[d]	—[d]
Hispanic	4.8	3.2	2.8	2.0

Source: SEER Cancer Statistics Review 1973 to 1997, National Cancer Institute, 2000.

[a] Rates per 100,000 person-years, age-adjusted using 1970 U.S. standard.

[b] SEER, National Cancer Institute. Based on data from eleven population-based registries in Connecticut, New Mexico, Utah, Iowa, Hawaii, Atlanta, Detroit, Seattle–Puget Sound, San Francisco–Oakland, San Jose-Montery, and Los Angeles.

[c] Based on data from the National Center for Health Statistics.

[d] Fewer than 25 deaths.

For all races combined and individually, the incidence and mortality rates were higher in males than in females (Table 26–2). The incidence rates for multiple myeloma among males and females combined in the 11 SEER registries were more than twice as high among blacks (9.5 per 100,000) as among whites (4.2 per 100,000). Although the data are based on small numbers, rates among Hispanics were slightly lower than among whites (3.9 per 100,000), whereas rates among Asians/Pacific Islanders (2.8 per 100,000) and American Indians (2.9 per 100,000) were substantially lower than those among whites. In as much as mortality rates for blacks, whites, and Hispanics are about two-thirds of the incidence rates, a similar racial and ethnic pattern is seen. However, mortality rates are lower than expected for Asians and Pacific Islanders (1.4 per 100,000) and higher than expected for American Indians (2.3 per 100,000), presumably owing to better survival among Asians and Pacific Islanders and poorer survival among American Indians.

International Patterns

International differences in multiple myeloma incidence, 1973 to 1977 to 1988 to 1992, as published in Volumes IV through VII of Cancer Incidence in Five Continents, are dramatic.[3–6] Generally increases in age-adjusted rates (world standard) over the two decades were noted for males in the U.S. SEER registry blacks and whites; the Canadian provinces of Quebec and British Columbia; Finland; Denmark; the United Kingdom; Spain; and Osaka and Miyagi, Japan (Figure 26–5A). For most countries, the time trends for females were similar to those for males, with consistent increases apparent in the U.S. SEER registry blacks and whites; British Columbia; Finland; Denmark;

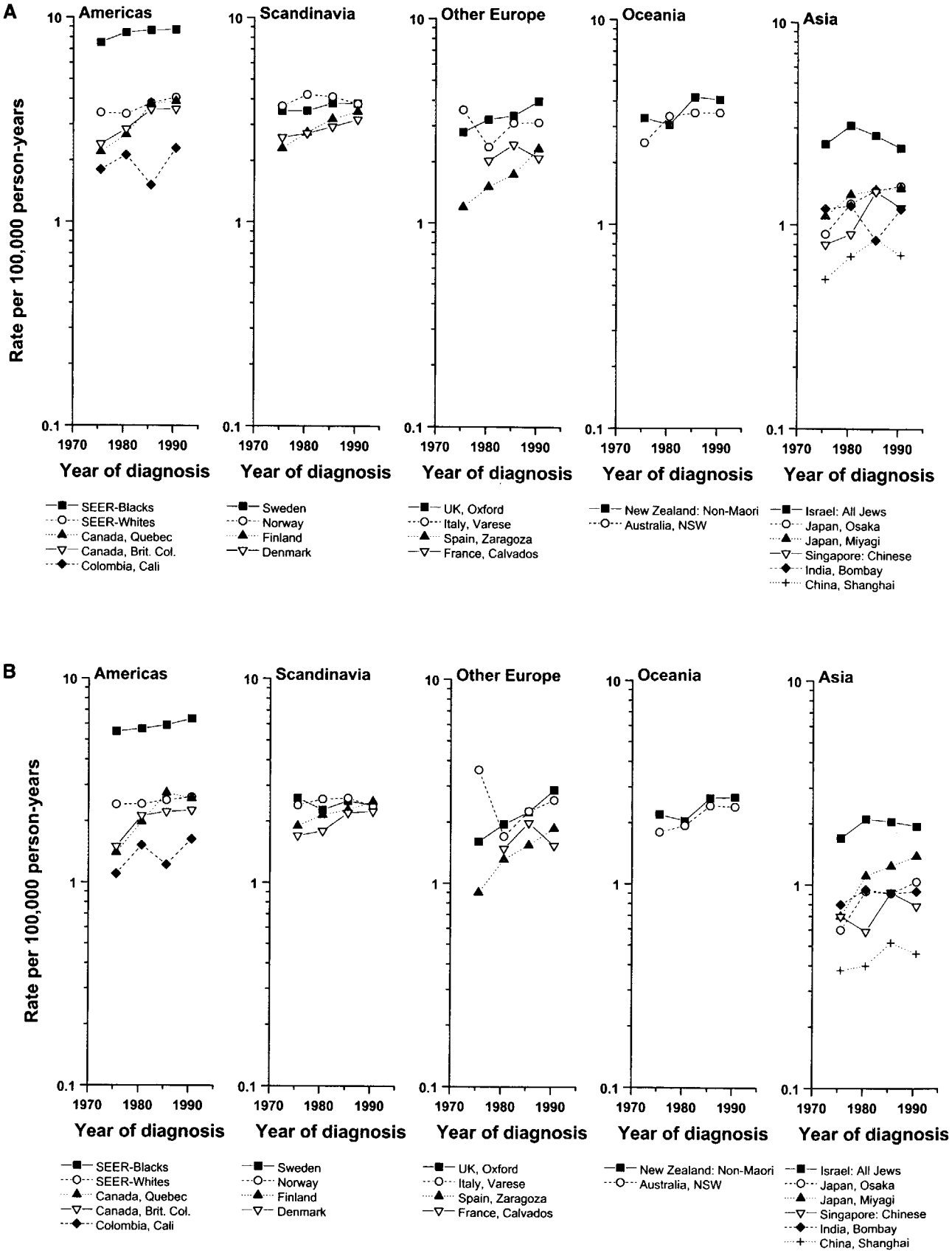

Figure 26–5. International incidence trends in age-adjusted (world standard) multiple myeloma rates by continent, 1973–77 to 1988–92. (A) Males; (B) Females.

the United Kingdom, Spain; and Miyagi, Japan (Figure 26–5B). Among both males and females, substantial increases were apparent in British Columbia, Spain, the United Kingdom, and Miyagi, Japan; less rapid rises occurred in SEER registry blacks and whites, Finland, Denmark, and Australia; and rates changed little in Norway, France, and Israel. Rates among males for the most recent time period, 1988 to 1992, were highest for SEER blacks (8.7 per 100,000), followed by New Zealand non-Maoris and SEER whites, and lowest in Shanghai, China (0.7 per 100,000). Rates were relatively low in Asia, except for Israel. Among females the rates for the time period 1988 to 1992 ranged from 6.3 per 100,000 for SEER blacks to 0.5 per 100,000 in Shanghai, China. In the most recent time period, rates varied more than 12-fold internationally and were higher in men than women in all selected populations; the male/female rate ratio varied from 1.08 in Italy to 1.60 in Norway.

ETIOLOGIC FACTORS

Ionizing Radiation

Most of the data on the effects of ionizing radiation on multiple myeloma risk come from studies of Japanese atomic bomb survivors[7–9] and studies of therapeutically exposed populations.[10–13] However, multiple myeloma also has been associated with lower levels of radiation exposure in several occupational studies.[14–17]

Atomic Bomb Survivors

Investigation of cancer incidence for the years 1950 to 1979[7] and cancer mortality for the years 1950 to 1985[8] among Japanese atomic bomb survivors suggested an increased multiple myeloma risk with increasing radiation dose. However, a more recent analysis of the incidence data for the years 1950 to 1987 yielded an estimated absolute risk of 0.08 cases per 10,000 person-years Sv (95 percent confidence interval less than 0 to 0.3), with no variation by sex, age at exposure, or time since exposure and no evidence of a significant dose–response relationship.[9] The most recent mortality analysis, covering the time period 1950 to 1990, yielded an estimated 0.17 excess risk per 10,000 person-years Sv (95 percent confidence interval, 0.02–0.40) for both sexes combined. Thus, the data available to date provide some support for an association between ionizing radiation from the atomic bombs and risk of multiple myeloma. However, additional years of follow-up evaluation will be required to elucidate the true nature of the association owing to the small number of exposed subjects who develop this cancer.

Diagnostic and Therapeutic X-Rays

Diagnostic x-ray exposure has not been clearly linked with multiple myeloma. Although several epidemiological studies reported no association between exposure to diagnostic x-rays and elevated risk of multiple myeloma,[18–22] other studies noted a positive association.[23,24]

Studies of the effects of therapeutic irradiation on myeloma risk have also been inconsistent. A few case-control interview studies have shown an excess risk of myeloma with radiation therapy[18] whereas others have not.[13,25] Elevated risks of multiple myeloma were reported in follow-up studies of patients receiving x-ray treatment for ankylosing spondylitis,[26,27] cervical cancer,[10] and metropathia hemorrhagica.[11]

Radiation-Related Occupations

Studies of occupationally exposed individuals have provided additional information on ionizing radiation and risk of multiple myeloma. An excess of myeloma deaths among American radiologists was first reported in the early 1960s.[28] More recently, myeloma risk was found to be twice as high among U.S. radiologists exposed to low-dose radiation than among physicians in other specialties[29]; however, no excess of myeloma was reported in a large study of Chinese diagnostic x-ray workers as compared with other medical specialists.[30]

Employment in nuclear facilities and risk of myeloma has been investigated in several cohort studies. Small excesses of myeloma mortality were reported among employees at Sellafield in Britain[14,31,32] and Hanford, in the United States, although the increase seen at Hanford did not reach statistical significance in a later follow-up study.[34] A combined analysis of cancer mortality data for over 95,000 nuclear industry workers employed at U.S. (Hanford), U.K. (Sellafield), and Canadian nuclear plants found an almost twofold significant increase for multiple myeloma.[16] Although a recent nested case-control study of workers employed at Hanford and Savannah River did not demonstrate an association between lifetime cumulative whole-body ionizing radiation dose and multiple myeloma, there was a significant effect of age at exposure, with positive associations between multiple myeloma and doses received at older ages.[17] An apparent trend of increasing risk of myeloma mortality with increasing estimated external radiation dose, noted among workers included in the National Registry for Radiation Workers in the United Kingdom, disappeared after excluding workers monitored for exposure to internal radiation emitters.[35]

Although several follow-up studies evaluated the risk of multiple myeloma mortality among military participants at nuclear weapon sites, the results were inconsistent. Elevated risk of myeloma was observed among military personnel in the United Kingdom[36] but not in New Zealand[37] or the United States.[38]

Residential Exposures

A recent study in Spain reported an excess risk of multiple myeloma mortality in the residential area near a nuclear power plant.[39] However, little evidence of an increased risk of multiple myeloma had been noted in previous investigations of the effect of residential proximity to nuclear facilities.[40–42]

Occupational Exposures

Farming and Other Agricultural Occupations

The majority of epidemiologic studies that evaluated the risk of multiple myeloma among farmers and other agricultural workers have reported positive associations.[43–53] A recent meta-analysis of 32 studies of multiple myeloma and farming published between

1981 and 1996 yielded an overall estimated relative risk of 1.23 (95 percent confidence interval, 1.14–1.32).[54] Exposures commonly experienced by farmers that might contribute to the increased risk of multiple myeloma include grain dusts,[55,56] engine exhausts and fuels,[57] farm animals,[58,59] and pesticides.[43,49,51,60] A number of epidemiologic studies have evaluated use of specific pesticides. Although some studies have noted positive findings with chlorinated phenoxy herbicides,[58] insecticides,[60] or DDT,[58,61] other studies observed no associations with specific pesticides.[47,62]

Metal Workers

Increased myeloma risk has been reported among workers in various metal occupations and industries,[63–67] although there are only limited data for exposure to specific metals.[58,68] Significantly elevated risks have been observed among smelter and metallurgy workers,[65] machinists,[63] nickel refinery workers,[66] and sheet metal workers.[67] In contrast, other studies have reported no notable associations with occupational metal exposures.[69–71]

Rubber Manufacturing

Some epidemiologic studies have suggested an association between multiple myeloma and employment in the rubber manufacturing industry.[19,72–76] However, overall results from a recent review of 12 cohort studies in nine countries, seven industry-based case-control studies, 48 community-based case-control studies in 16 countries, and 23 studies based on administrative data reported no excess risk for multiple myeloma with employment in this industry.[77] In addition, multiple myeloma was not found to occur in excess among workers exposed to styrene or butadiene in the rubber or the reinforced plastics and composites industry.[76,78–80]

Wood Products Workers

Several studies reported associations between myeloma risk and employment in the wood, furniture, and pulp and paper manufacturing industries.[81–84] Other studies showed little or no elevation in myeloma risk among wood product workers,[65,71,85,86] with the possible exception of forestry workers.[58]

Other Industries and Occupational Exposures

An association between multiple myeloma and employment in textile processing has been suggested in a few studies.[67,83,87,88] In contrast, two cohort studies of textile workers revealed no significant increase in deaths due to multiple myeloma.[89,90] Excess risks of myeloma among workers employed in the paint manufacturing industry have been noted in several studies.[64,91–94]

Other occupations linked with elevated risk of multiple myeloma in at least one study include nursing,[95] science technicians,[96] child care workers,[97] female workers exposed to silica,[98] railway carriage construction and repair workers,[99] meatcutters,[100] and firefighters.[49,101]

Specific Occupational Exposures

The relationship between benzene exposure and risk of multiple myeloma remains controversial.[102–104] Although benzene was replaced decades ago by toluene or xylene in most developed countries, it still remains as a low-level contaminant in gasoline, other solvents, and many products used or manufactured by the petroleum industry. Several studies have suggested benzene as a possible etiologic agent for multiple myeloma,[105,106] and one study reported an excess of myeloma among women residing within 7.5 kilometers of a petrochemical plant in South Wales.[107] In other studies, however, either the number of exposed myeloma subjects was too small to yield significantly elevated risk estimates or there was no elevation in risk.[108–113] In addition, no excess risk of myeloma was reported in a recent meta-analysis of data from 22 cohort mortality studies of petroleum workers in the United Kingdom, Canada, the United States, and Australia.[114]

Other Chemical Exposures

Excess myeloma mortality has been reported in some[115,116] but not all[117–119] investigations of chemical workers. Elevated risk of myeloma was linked to high levels of dioxin exposure in a follow-up study among residents of Seveso, Italy,[120] among fishermen residing on the east coast of Sweden,[121] and among verified clusters of multiple myeloma located near dioxin-contaminated bodies of water.[122] Exposure to organic solvents among aircraft maintenance workers and workers in the painting industry has also been linked to excess risk of multiple myeloma.[49,91,94,123,124] A positive association between myeloma and asbestos exposure has been reported in some[20,68,125] but not all[19,49,86,126] studies.

Lifestyle Factors

Cigarette Smoking and Alcohol Consumption

No relation with cigarette smoking has been reported for most epidemiologic studies of multiple myeloma.[19,55,68,88,127–133] However, significantly elevated risks were noted in a cohort of Seventh Day Adventists,[134] among women in the Third National Cancer Survey,[135] and for ex-smokers in a Swedish case-control study.[25] No epidemiologic study has reported a significant association between alcohol consumption and myeloma.[19,55,68,129,136]

Hair Dyes

There is conflicting evidence as to whether personal use of hair dyes increases the risk of developing multiple myeloma. Elevated risks of myeloma have been reported among women and men who used hair dyes in some[137–139] but not all[88,138] case-control studies, with the greatest risk observed among those using permanent hair dyes and dark hair coloring products.[139] No overall increased risk of myeloma among women who used permanent hair dyes was found in the American Cancer Society prospective mortality study; however, an elevated risk was observed among women who used black hair dye for 20 years or more.[140,141] Although the Nurse's Health Study lacked information on color of hair dye used, they found no excess risk of myeloma among women whose natural hair color was dark brown or black.[142] There are also inconsistencies in the epidemiologic literature concerning the relation between multiple myeloma and employment as a hairdresser, beautician, or cos-

metologist, with excess risks reported in some studies[88,143,144] but not in others.[83,138,145]

Diet and Nutritional Factors

Only a few epidemiologic studies have investigated the role of dietary or nutritional factors in the etiology of multiple myeloma. Elevated risk of myeloma has been linked with overweight and obesity in two cohorts of outpatients from a health maintenance organization in northern California[146] and in a case-control study conducted in three areas of the United States.[147] Protective effects have been reported in relation to frequent intake of vitamin supplements (especially vitamin C), fish, whole grains, and green vegetables (notably cruciferous vegetables).[147–150] Elevated risks have been reported for sources of animal fat, primarily liver and butter.[150]

Socioeconomic Status

The relation between socioeconomic status (SES) and multiple myeloma, whether measured by occupation, income, or education, has been evaluated in a number of epidemiologic studies. Two recent population-based case-control studies and a nested case-control study reported elevated risks of myeloma associated with lower SES.[19,151,152] In contrast, earlier studies observed either no association or a positive association between myeloma and SES, possibly owing to underascertainment of the disease in lower social class individuals.[81,135,153–156]

Medication Use and Medical Conditions

Medication Use

Although significantly elevated risks of multiple myeloma have been reported with use of laxatives, erythromycin, and mineral oil (in females but not males),[68,157,158] there is little evidence to suggest that any particular over-the-counter or prescription drug plays a important role in the etiology of multiple myeloma.[18,21,157] The assertion that chronic drug ingestion may predispose to myeloma[159] needs confirmation.

Monoclonal Gammopathy of Undetermined Significance

Monoclonal gammopathy of undetermined significance (MGUS) is an asymptomatic disorder characterized by a low proliferation of plasma cells and the presence of a monoclonal protein (M-protein) in the serum of persons without evidence of multiple myeloma, Waldenström's macroglobulinemia, primary amyloidosis, or other lymphoproliferative disorder.[160] It is well known that individuals with MGUS are prone to develop multiple myeloma. In a large Swedish MGUS cohort followed for 15 years, the standardized incidence ratio for myeloma was 34.3 (95 percent confidence interval, 24.8 to 46.2), as compared with the general population.[161] The actuarial probability for malignant transformation in two large series of MGUS patients was 31 percent at 20 years[162] and 40 percent at 25 years.[163] There are currently no clinical or laboratory findings that can predict which MGUS patients will develop a lymphoproliferative malignancy.

Chronic Immune Stimulation

A number of epidemiologic studies have investigated the hypothesis that repeated or chronic stimulation of the immune system may lead to multiple myeloma.[164] Risk of myeloma has been evaluated by assessing past history of individual immune-stimulating medical conditions, by examining categories of immune-stimulating medical conditions, such as autoimmune conditions and allergies, and by classifying medical conditions according to their biologically or immunologically related immune response mechanisms.[164–166] Although some studies have observed elevated risks for specific immune-stimulating medical conditions such as rheumatoid arthritis or for groups of medical conditions such as inflammatory diseases and chronic bacterial illnesses,[18,59,132,165,167,168] others have not.[65,68,166,169–172] Overall, the findings do not support a causal relationship between chronic immune stimulation and myeloma.[164,166,173,174]

Infectious Agents

The role of viruses or other infectious agents in the etiology of multiple myeloma is unclear. It has been suggested that immune-compromised persons may lack the ability to fight off viruses or other infections.[175] Many AIDS-related cancers have been associated with specific human herpesvirus infections,[176] and human herpesvirus 8 (HHV-8) has been detected in Kaposi's sarcoma and primary effusion lymphoma.[177] An increased incidence of myeloma was recently reported among people with AIDS in two large registry-based studies of AIDS,[175,178] and HHV-8 was found in the nonmalignant bone marrow dendritic cells of myeloma patients.[179] However, the role of HHV-8 in the pathophysiology of multiple myeloma is controversial[177] because most investigators have failed to detect a high seroprevalence of HHV-8 antibodies in patients with myeloma.[180–183]

Familial and Genetic Factors

Familial Aggregation of Cancer

An inherited component to multiple myeloma has been suggested by case reports of families with multiple affected members, especially siblings, and by observations that persons with multiple myeloma are more likely than others to have relatives with multiple myeloma or hematolymphoproliferative (HLP) cancer.[184–190] In case-control studies of multiple myeloma, investigators found two- to sixfold excess risks of myeloma among subjects who reported having a first-degree relative with myeloma and twofold excess risks among subjects with a history of HLP cancer in a first degree relative.[184,185,187,189] In the one study that investigated racial differences for myeloma, risk estimates for having a family history of HLP cancer tended to be higher for African Americans than for whites, although the difference in risks was not statistically significant.[185]

Genetic Factors

Although the etiology of multiple myeloma is unknown, there is growing evidence that certain cytokines, including inter-

leukin-6 (IL-6), Il-1β, and IL-10, play an important role in the growth of plasma cells and may be involved in the pathogenesis of myeloma.[191–193] In addition, recent studies have demonstrated that most if not all patients with multiple myeloma exhibit chromosomal abnormalities, but no specific abnormality common to all myeloma patients has been identified.[194] Typical abnormalities include a rearrangement involving the *IGH* gene at 14q32, with reciprocal translocations most often involving 11q13 and 4p16; chromosomal loss, most frequently monosomy 13; and structural rearrangement of chromosome 1.[194–197] Although *p53* gene mutations have been reported among multiple myeloma cell lines,[198,199] they are rarely found in myeloma patients and thus unlikely to play a major role as a tumor suppressor gene in myeloma development.[199–201]

CONCLUSION

Multiple myeloma is an intriguing malignancy. From an epidemiologic perspective, it is the only hematolymphoproliferative cancer, other than chronic myeloid leukemia and peripheral T-cell lymphoma,[202,203] that is characterized by higher incidence rates among blacks than whites. Although many investigators have studied the epidemiology of multiple myeloma, little is known about its etiology or reasons for the black excess in incidence.

The strongest associations have involved exposure to ionizing radiation and organic solvents and chemicals and employment in farming and agricultural occupations. Recent studies suggest that certain lifestyle and genetic factors, particularly low socioeconomic status, overweight and obesity, and familial aggregation of cancer may be linked to excess risk of multiple myeloma. Exposure to cigarette smoking and alcohol use do not appear to be related to myeloma, but the data on personal use of hair dyes remain controversial. Recent attention also has been focused on viruses and other infectious agents, but their role in the etiology of myeloma remains unclear.

There is growing evidence that certain cytokines and chromosomal abnormalities may be involved in the pathogenesis of multiple myeloma. These laboratory-based genetic measures need to be incorporated into future epidemiologic studies to better understand the complex relationships between genetic and environmental/lifestyle factors on the development of multiple myeloma.

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